STIC-ILL

From: Gabel, Gailene
Sent: Tuesday, July 02, 2002 5:26 PM
T : STIC-ILL
Subject: 09/738,049

Adams
17.50

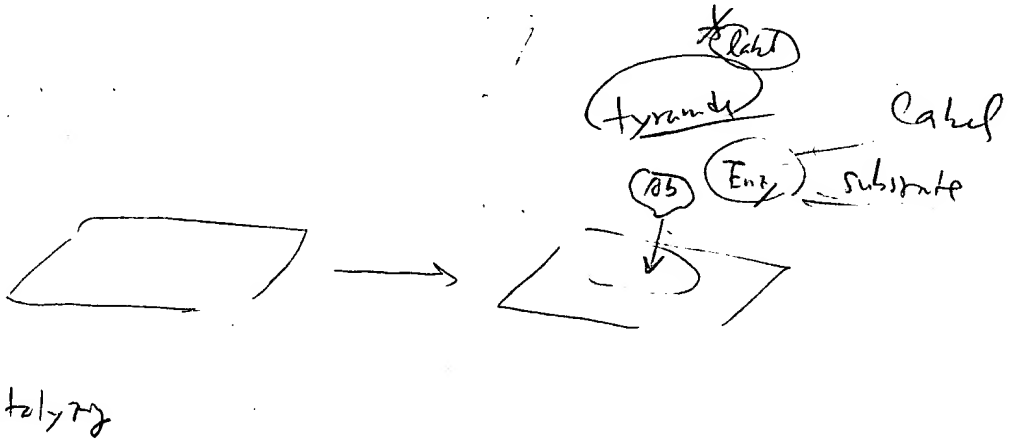
Please provide a copy of the following literature:

1) Li, Donghul, DNA adduct measurement by dual fluorescencelabeling, laser scanning cytometry and tyramide signal amplification. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 564.

2) Kaplan D, Enzymatic amplification staining for flow cytometric analysis of cell surface molecules, CYTOMETRY, (1 MAY 2000) Vol. 40, No. 1, pp. 81-85.

3) ~~Moritoyo T~~; Detection of human T-lymphotropic virus type I p40tax protein in cerebrospinal fluid cells from patients with human T-lymphotropic virus type I-associated myelopathy/tropical spastic paraparesis. JOURNAL OF NEUROVIROLOGY, (1999 Jun) 5 (3) 241-8.

Thanks a bunch
Gailene R. Gabel
7B16
305-0807



STIC-ILL 7393638 1073

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2) Kaplan D, Enzymatic amplification staining for flow cytometric analysis of cell surface molecules, CYTOMETRY, (1 MAY 2000) Vol. 40, No. 1, pp. 81-85.

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Gailene R. Gabel
7B16
305-0807

L6 ANSWER 7 OF 19 USPATFULL
ACCESSION NUMBER: 2001:226469 USPATFULL
TITLE: Detection method using luminescent europium-based protein stains
INVENTOR(S): Diwu, Zhenjun, Eugene, OR, United States
Patton, Wayne F., Eugene, OR, United States
PATENT ASSIGNEE(S): Molecular Probes, Inc., Eugene, OR, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6329205	B1	20011211
APPLICATION INFO.:	US 2000-652905		20000830 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-151684P	19990831 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Snay, Jeffrey
LEGAL REPRESENTATIVE: Skaugset, Anton, Helfenstein, Allegra
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1724
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the staining of amine-containing polymers, including including peptides, polypeptides, and proteins, in gels and on solid supports, using complexes of europium (3+).

DETD . . . fluorescent precipitate upon enzyme action (for example, the action of horseradish peroxidase upon diaminobenzidine, or enzyme action on a labeled **tyramide**), visible- or fluorescent-labeled microparticles, a metal such as colloidal gold, or a silver-containing reagent, or a signal that is released. . .

DETD TABLE 3

Representative specific binding pairs

enzyme	**enzyme** substrate
antigen	antibody
biotin	avidin (or streptavidin)
IgG*	**protein** A or **protein** G
carbohydrate	lectin
nucleic acid aptamer	**protein**

*IgG is an immunoglobulin

DETD The additional reagent may be used in conjunction with **enzyme** conjugates to localize the detectable response of the reagent. **Enzyme**-mediated techniques take advantage of the attraction between specific binding pairs to detect a variety of analytes. In general, an **enzyme**-mediated technique uses an **enzyme** attached to one member of a specific binding pair or series of specific binding pairs as a reagent to detect. . . pair are used. One member of the specific binding pair is the analyte, i.e. the substance of analytical interest. An **enzyme** is attached to the other (complementary) member of the pair, forming a complementary conjugate. Alternatively, multiple specific binding pairs may. . . complementary conjugate, or to both, resulting in a series of specific binding pairs interposed between the analyte and the detectable **enzyme** of the complementary conjugate incorporated in the specific binding complex.

DETD In another embodiment of the invention, a **protein** electrophoresis gel stained according to the method of the invention may be electroblotted to a filter membrane. After blocking non-specific. . . upon labeling and restaining. The staining of other poly(amino acid) labels, for example actin that is used to identify actin-binding

proteins, is readily accomplished in the same manner.

DETD . . . xenon lamps. These illumination sources are optionally integrated into laser scanners, fluorescence microplate readers, standard or mini fluorometers, microscopes, flow **cytometers**, gel readers, or chromatographic detectors.

L6 ANSWER 12 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:252362 BIOSIS
DOCUMENT NUMBER: PREV200000252362
TITLE: **DNA** adduct measurement by dual fluorescence labeling, laser scanning **cytometry** and **tyramide** signal amplification.
AUTHOR(S): Li, Donghul (1); Zhang, Weiqing; Chang, Ping; Thomale, Jurgen; Rajewsky, Manfred F.; Hittelman, Walter N.
CORPORATE SOURCE: (1) Institute od Cell Biology (Cancer Research), Univ of Essen, Essen Germany
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 564.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
TI **DNA** adduct measurement by dual fluorescence labeling, laser scanning **cytometry** and **tyramide** signal amplification.

L6 ANSWER 13 OF 19 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:348165 SCISEARCH
THE GENUINE ARTICLE: 309KW
TITLE: Enzymatic amplification staining for flow cytometric analysis of cell surface molecules
AUTHOR: Kaplan D (Reprint); Smith D
CORPORATE SOURCE: CASE WESTERN RESERVE UNIV, DEPT PATHOL, BIOMED RES BLDG, ROOM 926, 2109 ADELBERT RD, CLEVELAND, OH 44106 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: CYTOMETRY, (1 MAY 2000) Vol. 40, No. 1, pp. 81-85.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0196-4763.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 15

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: Flow cytometric analysis is a powerful technique for the single cell assessment of cell surface expression of selected molecules. The major deficiency of flow cytometry has been its relative insensitivity. Only molecules expressed in abundance have been readily observed.

Methods: We have developed an enzymatic amplification procedure for the analysis of cell surface molecules by flow cytometry. Transformed and nontransformed cells expressing MHC class I, CD5, CD3, CD4, CD6, CD7, CD34, CD45, MHC class II, Fas ligand, and phosphatidyl-serine were assessed.

Results: Our enzymatic amplification technology increased the fluorescence signal between 10 and 100-fold for all surface molecules tested.

Conclusions: Enzymatic amplification staining produces a significant enhancement in the resolving power of flow cytometric analysis of cell surface molecules. Using this technique, we have been able to detect the presence of molecules that could not be observed by the standard procedure. Cytometry 40:81-85, 2000. (C) 2000 Wiley-Liss, Inc.

ST Author Keywords: **tyramide**; flow **cytometry**; cell surface molecules; **enzymatic** amplification; Fas ligand; apoptosis; annexin V; phosphatidylserine

ANSWER 15 OF 19 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1999341464 MEDLINE
DOCUMENT NUMBER: 99341464 PubMed ID: 10414514
TITLE: Detection of human T-lymphotropic virus type I p40tax protein in cerebrospinal fluid cells from patients with human T-lymphotropic virus type I-associated myelopathy/tropical spastic paraparesis.
AUTHOR: Moritoyo T; Izumo S; Moritoyo H; Tanaka Y; Kiyomatsu Y; Nagai M; Usuku K; Sorimachi M; Osame M
CORPORATE SOURCE: Third Department of Internal Medicine, Faculty of Medicine, Kagoshima University, Japan.
SOURCE: JOURNAL OF NEUROVIROLOGY, (1999 Jun) 5 (3) 241-8.
Journal code: 9508123. ISSN: 1355-0284.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990903

AB We investigated the role of viral transcripts of human T-lymphotropic virus type I (HTLV-I) in the cerebrospinal fluid (CSF) cells and peripheral blood mononuclear cells (PBMCs) of patients with human T-lymphotropic virus type I-associated myelopathy (HAM)/tropical spastic paraparesis (TSP). To detect the HTLV-I p40tax **protein**, we developed a new sensitive method of immunohistochemistry combined with **tyramide** signal amplification and quantitative analysis. Seven patients with HAM/TSP were examined. As controls, four patients with other neurological diseases were examined; two of these patients were infected with HTLV-I and the other two were not. Both the CSF cells and PBMCs were reacted with a monoclonal antibody, Lt-4, for p40tax **protein**, followed by secondary antibody labeled with horseradish peroxidase. This was visualized by fluorescein directly labeled with **tyramide** and the number of positive cells was quantified with a Laser Scanning **Cytometer**. In the samples from patients with HAM/TSP, the HTLV-I p40tax **protein** was successfully detected by **tyramide** signal amplification, but not without it. In HAM/TSP patients, 0.04-1.16% of the CSF cells and 0.02-0.54% of PBMCs were positive for the HTLV-I p40tax **protein**, respectively. The expression of the HTLV-I p40tax **protein** in the CSF cells was more frequent than that in PBMCs in both HAM/TSP patients and HTLV-I carriers, and was also more frequent in the patients with HAM/TSP of shorter duration of illness. This technique could be a powerful tool to investigate the pathogenic mechanism of diseases associated with HTLV-I.

L6 ANSWER 16 OF 19 USPATFULL
ACCESSION NUMBER: 1998:69198 USPATFULL
TITLE: Compounds and method for synthesizing sulfoindocyanine dyes
INVENTOR(S): Bobrow, Mark Norman, Lexington, MA, United States
Erickson, Thomas Joseph, Carlisle, MA, United States
PATENT ASSIGNEE(S): E. I. du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5767287		19980616
APPLICATION INFO.:	US 1997-869032		19970604 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1996-687853, filed on 26 Jul 1996, now patented, Pat. No. US 5688966
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: McKane, Joseph
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 326
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel intermediates having an indolenine nucleus which are useful in the synthesis of fluorescent sulfoindocyanine dyes are described. Dyes synthesized using such intermediates do not contain a reactive group that will covalently attach to a target molecule at an amine- or hydroxy-containing site. Rather, these intermediates are linked to an enzyme substrate or a member of a specific binding pair. Also included are tyramide-containing sulfonidocyanine dyes.

SUMM Use of fluorescent labels with antibodies, **DNA** probes, biochemical analogs, **lipids**, drugs, **cytokines**, cells and polymers has expanded rapidly in recent years due, in part, to the availability of new fluorescent labeling reagents.

SUMM . . . labeling reagents based on sulfoindocyanine dyes. They contain succinimidyl ester reactive groups and can be readily conjugated to antibodies, avidin, **DNA**, **lipids**, polymers, and other amino-group containing materials. These sulfoindocyanine dyes generally are formed when a quaternized indolenine nucleus containing a carboxyl. . .

SUMM Chao et al., **Cytometry**, Vol. 23, pages 48-53 (1996), describes a fluorescent horseradish peroxidase substrate, Cy3.29 and its use in an **enzyme**-based signal amplification system (catalyzed reporter deposition, CARD). Cy3.29 **tyramide** was synthsized by utilizing a succininide ester intermediate.

DETD **Tyramide**-containing sulfoindocyanine dyes made using the process of the invention can be used as reporter substrates in an **enzyme**-based signal amplification system called catalyzed reporter deposition ("CARD"). The CARD system constitutes the subject matter of U.S. Pat. No. 5,196,306. . . hereby incorporated by reference. Use of such dyes in connection with the CARD system is described in Chao et al., **Cytometry**, 23:48-53 (1996).

DETD Structures of **tyramide** containing sulfoindocyanine dyes which can be synthesized using the above-described process include: ##STR7## wherein m is 1, 2 or 3.

L6 ANSWER 19 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3
ACCESSION NUMBER: 96028606 EMBASE
DOCUMENT NUMBER: 1996028606
TITLE: Immunofluorescence signal amplification by the enzyme-catalyzed deposition of a fluorescent reporter substrate (CARD).
AUTHOR: Chao J.; DeBiasio R.; Zhu Z.; Giuliano K.A.; Schmidt B.F.
CORPORATE SOURCE: Ctr. for Light Microscope Imaging, Carnegie Mellon University, 4400 Fifth Ave.,Pittsburgh, PA 15213, United States
SOURCE: Cytometry, (1996) 23/1 (48-53).
ISSN: 0196-4763 CODEN: CYTODQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
005 General Pathology and Pathological Anatomy
025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Progress has been made in improving the immunohistochemical detection of antigens for imaging and flow **cytometry**. We report the synthesis of a novel fluorescent horseradish peroxidase substrate, Cy3.29-**tyramide**, and its application in an **enzyme**-based signal amplification system, catalyzed reporter deposition (CARD). The catalyzed deposition of Cy3.29-**tyramide** was used to detect cell surface markers such as CD8 and CD25 on tonsil tissue and human lymphocytes. We compared the fluorescence CARD method to standard indirect immunofluorescence detection methods and found that an amplification of up to 15-fold was possible with CARD. The detection of the **intracellular protein** myosin II in fibroblastic cells and rabbit serum **proteins** blotted onto nitrocellulose was also improved. Thus, fluorescent CARD is a simple modification that can be made to standard immunofluorescence staining protocols to enhance significantly the detection of antigens.

L8 ANSWER 10 OF 25 USPATFULL
ACCESSION NUMBER: 2001:202455 USPATFULL
TITLE: Luminescent protein stains an their method of use
INVENTOR(S): Bhalgat, Mahesh K., Saint Louis County, MO, United States
Diwu, Zhenjun, Lane County, OR, United States
Haugland, Richard P., Lane County, OR, United States
Patton, Wayne F., Lane County, OR, United States
PATENT ASSIGNEE(S): Molecular Probes, Inc., Eugene, OK, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6316267	B1	20011113	
APPLICATION INFO.:	US 1999-429739		19991027	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-105839P	19981027	(60)
	US 1998-113828P	19981223	(60)
	US 1999-126346P	19990326	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Snay, Jeffrey
LEGAL REPRESENTATIVE: Skaugset, Anton, Helfenstein, Allegra
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 2116
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the staining of poly(amino acids), including peptides, polypeptides and proteins in gels and on solid supports, using neutral or anionic complexes of transition metals.

DETD . . . are physically separated before or while it is combined with the staining mixture, including but not limited to separation by **flow cytometric**, electrophoretic, or microfluidic methods. Where the components of the sample mixture include cells, the cells are optionally separated based on. . .

DETD Destaining of stained gels is typically not necessary for luminescent detection of **proteins** using the metal complexes of the invention, although for certain staining formulations containing methanol/acetic acid, destaining typically improves poly(amino acid) detection in gels. For example, while staining of **proteins** in polyacrylamide gels is typically accompanied by some background staining of the gel matrix, such background staining can be reduced. . . does not contain the staining metal complex. This incubation typically removes dye from the gel background, with little loss of **protein** staining. Stained gels may also be washed briefly after staining to prevent transfer of the staining metal complex to other. . .

DETD . . . useful for identification of other components in the sample mixture, such as a nucleic acid stain, or a stain for **lipids** or carbohydrates. Or, the additional reagent is a detection reagent designed to interact with a specific portion of the sample. . .

DETD . . . to provide a detectable response include, but are not limited to, a visible or fluorescent dye, a chemiluminescent reagent, an **enzyme** substrate that produces a visible or fluorescent precipitate upon **enzyme** action (for example, the action of horseradish peroxidase upon diaminobenzidine, or **enzyme** action on a labeled **tyramide**), visible or fluorescent labeled microparticles, a metal such as colloidal gold, or a silver-containing reagent, or a signal that is. . .

DETD . . . metal complex such that the labeling of some or all poly(amino acids) exhibits quenching. Alternatively, the additional reagent is

another **protein** stain (such as CBB or silver stain) such that labeling of the poly(amino acids) is enhanced by the colocalization of. . .

DETD . . . the present invention can be selected to allow simultaneous or sequential observation of poly(amino acids) and nucleic acids such as **DNA** and **RNA**.

DETD TABLE 2

Representative specific binding pairs

enzyme	**enzyme** substrate
antigen	antibody
biotin	avidin (or streptavidin)
IgG*	**protein** A or **protein** G
carbohydrate	lectin

*IgG is an immunoglobulin

DETD The additional reagent may be used in conjunction with **enzyme** conjugates to localize the detectable response of the reagent. **Enzyme**-mediated techniques take advantage of the attraction between specific binding pairs to detect a variety of analytes. In general, an **enzyme**-mediated technique uses an **enzyme** attached to one member of a specific binding pair or series of specific binding pairs as a reagent to detect. . . pair are used. One member of the specific binding pair is the analyte, i.e. the substance of analytical interest. An **enzyme** is attached to the other (complementary) member of the pair, forming a complementary conjugate. Alternatively, multiple specific binding pairs may. . . complementary conjugate, or to both, resulting in a series of specific binding pairs interposed between the analyte and the detectable **enzyme** of the complementary conjugate incorporated in the specific binding complex.

DETD . . . upon labeling and restaining. The staining of other poly(amino acid) labels, for example actin that is used to identify actin-binding **proteins**, is readily accomplished in the same manner.

DETD . . . and Nd-YAG lasers. These illumination sources are optionally integrated into laser scanners, fluorescence microplate readers, standard or mini fluorometers, microscopes, **flow cytometers**, gel readers, or chromatographic detectors.

DETD . . . or the use of currently used instrumentation such as laser scanning devices, fluorometers, photodiodes, quantum counters, epifluorescence microscopes, scanning microscopes, **flow cytometers**, fluorescence microplate readers, or by means for amplifying the signal such as photomultiplier tubes. When recording the optical response of. . .

DETD The instant metal complexes have demonstrated utility as a single color viability stain when used in conjunction with **flow cytometry** or luminescence imaging. While not wishing to be bound by theory, it appears that nonviable cells (having compromised cell membranes). . .

DETD Differentiating Live and Dead Cells by **Flow Cytometry**

DETD . . . microcentrifuged, washed twice with PBS and re-suspended in the same. Each group of cells is then transferred to a separate **flow cytometer** tube. To the unstained is added a 5 .mu.M solution of the dead cell stains SYTOX GREEN stain (Molecular Probes,. . .

DETD The cell suspensions are analyzed by **flow cytometry**: Data acquisition is performed using a Becton-Dickinson FACS Vantage **flow cytometer** (San Jose, Calif.). The 488-nm line of an air-cooled argon-ion laser is used at 100 mW. Sample acquisition and analysis. . .

DETD . . . 90 and 100%, respectively. The mixtures are prepared in a 100 .mu.L volume, stained with Compound 1 and analyzed by **flow cytometry** as above. **Flow cytometric** analysis of the mixtures shows measured dead cell percentages of 2, 13, 31, 46, 65, 76 and 96% respectively.

CLM What is claimed is:

26. A method, as claimed in claim 25, wherein said separating step is

accomplished by **flow cytometric** methods, electrophoretic methods, or microfluidic methods.

27. A method, as claimed in claim 25, wherein said sample mixture comprises cells, said separating step is accomplished by **flow cytometric** methods, and the detectable optical response is correlated to cell viability.